THE JOURNAL OF THE CANADIAN ASSOCIATION OF RADIOLOGISTS

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EDITORIAL

FALLOUT AND THE RADIOLOGIST

Recently there has been a wave of publicity over the supposed harmful effects of small amounts of radiation, particularly radioactive fallout. It has attracted much of the free-floating anxiety present in many people in the community. Controversy between workers in the fields of genetics, biology, chemistry and physics has intensified the anxiety. The radiologist is one of the few people in the community who works in both biological and physical fields and who, by training and experience, is equipped to make reasonable decisions about radiation hazards. Should he not take a more active part in directing community thinking on this matter? Is he evading his medical and social responsibilities if he does not do so?

Radio-active fallout is partly natural and partly the result of atom and hydrogen bomb explosions. Megaton explosions put radio-active particles into the stratosphere where they spread widely and where they stay for five to ten years. Kiloton explosions put radio-active particles into the trophosphere where they spread in a band around the earth in the latitude of the parent explosion and from which they fall in about a month. The particles fall to earth mostly with rain and snow.

Some of the radio-active atoms in fallout enter biological processes and may enter man. Of these, the most important are Strontium-90 of half-life 25 years and Caesium-137 of half-life 33 years. Less important are Strontium-89 of half-life 53 days, Carbon-14 of half-life 5,726 years and Tritium of half-life 12.5 years.

Some of the Strontium-90 ingested by humans is absorbed and deposited in the bones where it stays for a long, but as yet undetermined time. Direct analysis of human bones from the Northern Hemisphere in 1957-1958 showed an average concentration of Strontium-90 of 0.2 micro-micro-Curie per gram of calcium in adults and 1.0 micro-micro-Curie per gram of calcium in children. These concentrations are two ten-thousandths and one one-thousandth respectively of the Maximal Permissable Concentration (M.P.C.) established by the International Commission on Radiological Protection (I.C.R.P.). These concentrations of Strontium-90 in adults and children produce radiation doses of 0.6 millirem to 3 millirem per year respectively to the bones and little, if any, dose to the gonads. This is 1.5% and 8% respectively of the average dose of 39 millirem per year that we all receive from naturally occurring radium in our bones. Caesium-137 has a fairly uniform distribution in the body but is eliminated in 6-8 months. It produces a total body dose of about 2 millirem per year. The other assimilated and non-assimilated fallout products add a further total body dose of approximately 2 millirem per year.

Therefore, the whole body dose due to radio-active fallout is 2.5-5 millirem per year at the present time. This is about 5% of the whole body dose of 100 millirads per year that the average man gets from himself and his natural surroundings. It is approximately 2% of the whole body dose of 300-500 millirads per year that people living in mountainous regions receive from their natural surroundings. It is less than 1% of the whole body dose of approximately 1000 millirads per year that people living in Travancore and parts of Brazil receive from their natural surroundings.

The I.C.R.P. has set the Maximal Permissible Dose (M.P.D.) of external radiation for X-ray and radium workers at 15 rads per year, believing that this amount of radiation will produce no detectable harm to the individual during his lifetime. This figure seems to be well within the limits of safety as shown by a recent survey of 1,377 British radiologists from the year 1897 to the year 1957. These radiologists showed no significant reduction in life span or increase in leukemia, even though they included many of the pioneers in radiology who received very large doses of radiation.

D. L. McRae, M.D.

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THE GORDON RICHARDS MEMORIAL LECTURE ON THE EFFECT OF IONIZING RADIATION ON THE CELL*

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It is an honour to be asked to give this Gordon Richards Memorial Lecture to the Canadian Association of Radiologists. I accepted with some reservation, as neither did I have the good fortune to know or come in contact with Dr. Gordon Earle Richards, nor am I a radiologist or radiobiologist. I assume you asked me to speak to you as a biologist, in the broadest sense of the term, who is interested in the reactions of the cell to alteration in either its external or internal environment.

I was aware that Dr. Gordon Richards was the Professor of Radiology at the University of Toronto, and a leading Canadian and international figure in the field of the radiotherapy of cancer. After consulting the previously published Gordon Richards Memorial Lectures, I am indebted particularly to those of Professor Jones in 1955[15] and Dr. Cosbie in 1957[7] for giving me a better understanding of this important figure in the history of medicine in Canada. Gordon Richards' son, Dr. A. J. Richards of Regina, has helped me to obtain a more intimate picture of his father. Dr. Gordon Richards had an inquiring and tidy mind, and a marked interest in experimental instrumentation, so I am sure that were he alive he would be greatly attracted by some recent findings in fundamental radiobiology. This is the subject which I would like to discuss with you today. To clarify our objectives I suggest that we confine ourselves to the effect of ionizing radiation on the individual cell, and the sub-cellular particles. I am very conscious of the complexities of the interactions between cells in the whole animal, and we all realize that the effects of total body irradiation are perhaps more than a summation of the effects on the individual cells.

Radiation and Cells

It might be as well at the beginning to spend a few minutes reviewing some of the fundamental facts about ionizing radiation[2,9], and about cells[11]. To those of you who deal with these facts in your day-by-day work I apologize, but consider it important that we begin with a clear understanding of these fundamentals. Alpha- and beta- particles are charged. They are quite different in mass. They have relatively low penetrating powers, but can produce marked ionization over short paths. On the other hand the X-and gamma-rays are non-particulate in nature, will penetrate a considerable depth of tissue, and produce their effects by knocking electrons out of the orbits of atoms in their paths. Some of the energy of the radiation is transferred to these electrons, which in their turn produce ionizations in varying volumes of tissue. It should be emphasized that all of these radiations can produce direct ionization in atoms in their path in tissue. The number of secondary ionizations produced exceeds by some thousand fold the direct hits on atoms, and thus become the more important factor in the production of biological effects.

If one considers the passage of different types of radiation through a virus particle, and assumes that one ion pair is sufficient to inactivate the virus, then the greatest efficiency comes from high voltage radiation which produces relatively few ion pairs per micron. At the other end of the scale the alpha-particle produces an intense ionization over a short distance, but many of these ionizations are not effective since only one of the ion pairs is necessary to inactivate the virus[9]. This introduces two terms which we should understand: one is the *linear energy transfer*, or LET, which has to do with the number of ion pairs released per micron of path, and it has been calculated that each ion pair is equivalent to 35 eV. The linear energy transfer in the case of high energy X-rays is small, whereas with alpha-radiation it is high. The other concept is that of the *relative biological efficiency*, or RBE. In this particular instance of a virus particle requiring only one "hit" for inactivation, the relative biological efficiency of the alpha-radiation is low, as many more hits than are necessary are concentrated in the target volume.

It is possible that ionization produced in the medium may be of greater biological importance than the direct impingement of the

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radiation on some specific molecule or centre. Let us consider the effects of irradiation on the most common constituent of a cell, water. When a high speed electron passes through water, either from an electron beam or from the ejection of an electron by electromagnetic radiation, it produces a chemical excitation of many of the water molecules through which it passes. In a certain number, the radiation actually may knock an electron from the outer shell of the water molecule, leaving a positively charged molecule of water; both the electron and positive ion can react further, producing radicals with a positive or negative charge, or electrically neutral. All of these radicals are highly reactive chemically and thus the name "active radical", such as the hydrogen, hydroxy or perhydroxy radical. These active radicals have extremely short lives, as they react almost instantly with the first molecule they encounter. The molecule with which they interact undergoes a marked chemical change, which may be an oxidation or the disruption of a chemical bond. Even if a cell or compound in the direct path of radiation is missed it has a good chance of being attacked by one or more of these active radicals, which potentiate the effect of radiation in biological systems[2].

Let us turn our attention for a moment to the cell. You will recall from your elementary histology the division of the cell into nucleus and cytoplasm, the nucleus containing the chromatin threads, and the cytoplasm certain particulate matter such as mitochondria and secretory granules. The electron microscope has given new depth to our vision of the cell. Certain smaller granules in the cytoplasm which today are referred to as microsomes are of the order of 50 to 100 mμ in size, which brings them within the range of a virus particle[11]. We will have more to say later about the structure of chromosomes, viruses, and of the nucleic acids.

Damage to chromosomes and genes

The genetic characteristics of an organism are associated with a biological entity called the gene. The genes lie in pairs, referred to as alleles, along the chomosomes. Any particular hereditary characteristic is the result of interplay between the allele pair, one of the alleles being inherited from each parent. If a particular characteristic is inherited as a dominant it becomes obvious in the next generation. If it is inherited as a recessive characteristic it may remain obscure for several generations until the counterpart recessive allele is inherited from another parent, when the two recessives together produce the characteristic. The inheritance of recessive characteristics is important in a consideration of radiation and the production of mutations[1].

There is considerable experimental evidence for the assumption that the genes are composed of a chemical substance called deoxyribonucleic acid. DNA is a very large molecule, of the same order of size as the viruses, that is with molecular weights in the millions and particle sizes of 20-50 mμ[2]. The components of DNA are organized in a helix structure, containing many bonds that might be disrupted by ionizing radiation, or by active radicals. It is fundamental to the concept of the gene that it must be a self-reduplicating particle, and thus able to direct its own synthesis.

The typical description of a chomosome is that seen in the fruit fly drosophila. Examination of fixed and stained giant chromosomes shows darkly stained areas containing DNA, and lightly stained areas of the protein which binds the DNA together in the chromosome structure. In the inter-mitotic or resting stage of cells the chromosomes are not visible. During the prophase of mitosis the chromatin material becomes organized into chromosomes, and each chromosome splits longitudinally to give two daughter chromosomes containing the identical genetic material of the parent. This is better seen in the metaphase and in the anaphase. These reduplicated chomosomes separate into two different groups, one of which will go to each daughter cell as seen in the final or telophase stage. At the end of telophase the two daughter cells separate, and once more the chromatin material becomes discrete in the nucleus until it is concentrated in a subsequent prophase stage.

One of the first described effects of radiation on the cell was interference with mitosis and damage to chromosomes[19]. It has been known for some time that a cell actually in the process of mitosis is fairly resistant to radiation, and the more sensitive phase in the cycle is the so-called resting or inter-mitotic phase. It will be appreciated that "resting" is a morphological term, and this is probably the period when maximum DNA synthesis is proceeding for the reduplication of the gene and chromosome material, in preparation for the prophase of mitosis. Indeed a recent study, measuring the rate of incorporation of DNA precursors into bone marrow cells irradiated in culture, suggests that some mechanism which precedes the actual DNA synthesis is even more radiosensitive than the mechanism whereby DNA is synthesized[18].

If very large doses of radiation are given the cell is immediately killed. However with smaller doses there is an inhibition of mitosis, but subsequently the cell may recover and go into mitosis. If the percent of cells in mitosis is being measured, then the depression of

mitosis is followed by an apparent stimulation, as in the recovery period the inhibited cells go into mitosis, as well as the ones which would normally proceed this way[30]. There may be a resultant stickiness of chromosomes, and delay in mitosis, but at certain doses of radiation the cells can recover, and subsequent generations go on to perfectly normal mitosis.

Some cells studied after irradiation exhibit abnormal chromosome figures during mitosis, depending on the dose and sensitivity. An actual chromosome break is the usual initial abnormality produced, but it should be realized that many of these breaks can be reconstituted with no apparent subsequent chromosomal or genetic abnormality. In some instances the break persists, and may interact with other chromosomes to form abnormal fragments and bridges[2].

With marked chromosome abnormalities the cell may not be able to enter subsequent divisions, and dies. With less structural and functional damage cell division may be possible, and the error is transmitted to subsequent generations. Since the chromosome break may be associated with a loss of some genetic material, and since the effect of genes is related to their position, as well as to their presence, some of these abnormal cells may be classed as mutations. We must remember that a mutation in the genotype must be a dominant to become apparent at once in the phenotype, that is, in the apparent characteristics of the individual.

It has been mentioned that the mitotic cycle is at a maximum of radiosensitivity during the interphase, when the chromosomes are not observable under the microscope as discrete structures. However by an ingenious microtechnique Zirkle and his colleagues[4,33] have been able to direct a micro beam of radiation on to a specific part of a cell. The radiation can be concentrated into a beam of approximately 5μ in diameter. Such a beam may be focused onto a cell during mitosis, and a specific part of a chromosome, or of the mitotic spindle, subjected to radiation. In this way the locus of the chromosome break can be predicted, rather than being left to the random chance of total cell irradiation.

Until recent years it was assumed that these chromosome breaks were produced by the disruption of an intact chromosome by the irradiation. It had been calculated that some 700 eV were required to produce the break, and this would be the result of the action of twenty ion pairs[19]. Since a chromosome would be something of the order of 0.1 μ in width this would then mean at least 200 ion pairs per μ — the type of radiation produced by alpha-particles. Subsequent experiments established that the passage of a single alpha-particle through the nucleus of a cell would always produce a chromosome abnormality[22], and it was unlikely that every time a single particle passed it would physically intersect with a chromosome. Furthermore the greatest sensitivity to production of chromosome breaks was at a time when the chromatin material lay discretely throughout the nucleus, rather than when the chromosomes were well formed during mitosis. Perhaps the most damaging evidence against the concept of the mechanical fracture of the chromosome was the fact that the relation between irradiation and chromosome breakage exhibited the "oxygen effect". In the absence of oxygen during irradiation approximately a third of chromosome breaks are observed when compared to the number produced by the irradiation in the presence of oxygen[10]. The present view is that, rather than the fracture being produced in a formed chromosome, a lesion is produced in the biochemical mechanism responsible for the synthesis of DNA and chromosomes[17]. Thus the chromosome break represents not so much the fracture of a chromosome as the absence of the material required for the formation of a specific locus on the chromosome.

With low doses of radiation a cell is produced with no apparent nuclear or chromosomal abnormalities, but the subsequent generations of which exhibit certain genetic abnormalities. These "gene mutations" are alterations produced by the passage of ionizing radiations through the cell, and one assumes by the interaction of an ion pair or "active radical" with the DNA molecule associated with that particular gene. This may result either in gene deletion or gene modification[19]. You will realize that if the site of radiation has been the gonads the stem cells may be the site of the mutation, and if so all successive gametes produced will manifest this mutation. Further, as has been emphasized, if this mutation is in a recessive gene its presence may not become manifest for several generations. One of the simplest gene mutations to observe as a result of radiation is the production of the so-called dominant lethal. This is the modification of a gene which controls some particular process necessary for continued existence, and in its absence the cell or organism dies. The possibility of a gene mutation by low levels of radiation is perhaps the most worrisome of all the biological effects produced by radiation since it is passed on to all subsequent generations. Unfortunately most gene mutations are deleterious. Many of these mutations are associated with mental deficiency, which is much more alarming in modern civi-

lization than physical deformity. Recent works suggest that radiation induced mutations are not independent of dose rate[23].

Cytoplasm

So far we have been concentrating our attention on the nucleus of the cell, and have not considered the cytoplasm, except to indicate that with exposure to very high levels of radiation immediate cell death may result. It is perhaps of interest at this point to indicate that the lethal dose of irradiation for a cell varies markedly with different species[1]. Some unicellular organisms actually require as high as 300,000 r. to produce an LD 50. We can simply report this as an interesting fact that has emerged from radiobiological studies, and we cannot explain the reason for this phylogenetic difference. It is not felt that this wide variation in LD 50 negates the use of some of the simpler organisms, which require higher dosages, in studies of fundamental radiobiology.

Some quantitative concept of the different radiosensitivity of nucleus and cytoplasm may be obtained from studies on the egg of a parasitic wasp. It has been shown that whereas the nucleus of the egg can be inactivated by the passage of one alpha-particle, for an LD 50 in cytoplasm 16 x 10^6 alpha-particles per egg are required[5]. There are probably many reasons for this difference, but one is suggested by a consideration of molecular distribution in the cell. The number of DNA molecules in the nucleus of a haploid yeast cell is of the order of 2000, and possibly each of these molecules represents a highly specific function which cannot be taken over by another if the first is destroyed by radiation. On the other hand the number of physiologically active protein particles in the cytoplasm greatly exceed this number, and possibly are represented in depth, i.e., any specific function may be taken over by one of several similar particles[29]. If yeast cells are irradiated in the wet and dry states, and assayed for certain enzymes, it is found that the ionizing radiations are 2, 20 or 100 times as effective in the wet state[14]. The LD 50 of the diploid yeast cell is 20,000 r. — this dose will inactivate only 1% of the enzyme molecules in the cytoplasm[19].

These survival studies are borne out by experiments with nucleated and enucleated fragments of cells, as well as by experiments with nuclear transfer. The marine algae Acetabularia is a very large single plant cell. Thus it is relatively easy to remove the nucleus from a fragment, and study the effects of radiation on cytoplasm less the nucleus. Under these circumstances the enucleate fragment is much more radio-sensitive than is the intact cell[3]; similar observations have been noted on amoeba[24]. This may be a reflection of recovery from radiation, as it has been shown that the enucleate fragment of Acetabularia can continue to synthesize protein as long as the cytoplasmic ribonucleic acid is present. However the cytoplasm is unable to replace this ribonucleic acid in the absence of the nucleus[28].

The results of Puck and Marcus on the effects of irradiating cells in culture are of interest. Many of these cells will die, while others will be severely injured so they can no longer divide, but continue to increase in mass and become giant cells. This appears to result from damage to the genetic apparatus, but with continued activity of the cytoplasmic mechanism for protein synthesis[21].

Effects of radiation on viruses

We have mentioned that the genetic units of the chromosomes are assumed to be macromolecules of DNA (deoxyribonucleic acid), and have indicated that one of the characteristic biological features of the gene is the property of self-duplication. Other biological units which share this property of self-duplication, and are composed of nucleic acids, are the viruses. When the virus is a type which attacks bacteria we refer to it as a bacteriophage. Wendell Stanley startled the biological world in the mid 1930's with the demonstration that the tobacco mosaic virus could be prepared as a pure crystalline ribonucleoprotein, the virus being composed of a central core of nucleic acid, surrounded by an envelope of protein[26]. Macromolecular particles which can exhibit some of the manifestations of life make excellent test material for studying fundamental radiobiological mechanisms.

A bacteriophage attaches itself to a bacteria by its tail, and then extrudes into the bacteria the DNA contained inside the phage. Utilizing the energy mechanisms and building blocks of the bacteria the virus DNA molecules are able to direct the further synthesis of their own DNA, as well as more of the protein overcoats[6]. When sufficient of these phage particles accumulate inside the bacterium lysis occurs, and the phage is released into the medium. Thus one particle can become many. Bacteria may be subjected to doses of radiation that prevent their multiplication, but they continue to support the growth of T_1 and T_2 phage — since the phage relies on the energy mechanism of the cell these must continue to function after colony formation has ceased[20]. It has been shown that infectivity and disease production resides in the DNA or RNA core of a virus, whereas the antigenic properties appear to be part of the protein overcoat. More recent experiments

suggest that the biological response to a virus may be brought about by infection with the nucleic acid molecule only[8].

Much of the experimental work supporting the direct action of radiation on target areas was conducted with viruses, in particular viruses in a dry or frozen state[19]. The characteristics of varying types of radiation, and the resultant biological effects on the virus gave rise to the view that the production of one ion-pair in a virus particle was all that was required for inactivation of the particle, and in some instances the production of one ion-pair in a bacterium was all that was necessary for death of the bacterium. The use of dried or frozen material reduced the chance that the biological effect was the result of active radicals produced by the irradiation of water. The pioneering work in this field was done by the English physicist, Douglas Lea, and has been continued by many others, in particular by Pollard of Yale. By using radiation with different characteristics, and observing various biological "markers" it was noted that a lower dose of radiation was required to inactivate a virus than the dose required to destroy the antigenic properties. The radiation physicist was able to predict certain things about the size and shape of these vital macromolecules which were subsequently confirmed by direct observation in the electron microscope. For example Pollard and his associates have recently shown that with the T_1 phage their results are consistent with a DNA chain length of 1 micron for protein synthesis, and a chain length of 2.5 microns for infective centres[31]. In studies on the properties of the Newcastle disease virus some of the findings suggest, for example, that the virus is approximately 1000 Angstrom units in diameter, but infectivity is associated with a 560 Angstrom unit core, around which are coated a protein hemolysin and a protein hemagglutinin of different sizes and shapes[32]. Thus radiation biology has led to the development of a sensitive and useful analytical tool (the radiation "probe") in considering the structure of certain of the most interesting biologically active macromolecules.

Direct and indirect effects of ionizing radiations

At the time of publication of the first edition of Lea's book "Action of Radiations on Living Cells" it appeared that the simplest and most valid explanation for the effects of radiation on the cell was to assume direct hits on certain sensitive target volumes, originally suggested by Crowther in 1924. However since 1947 increasing attention has been given to the place that active chemical radicals may play, particularly in the more complex system of the living cell. Whereas the model system of the virus particle suggested that the relative biological efficiency of alpha-radiation is much lower than that of a gamma- or X-ray, the reverse is known to be true when intact cells are exposed to the effects of radiation. By and large alpha-radiation has a higher RBE than gamma- or X-rays[25]. The oxygen effect is reduced with alpha-particles[13], but this may be the result of a high concentration of hydroxy radicals over relatively few microns. Active radicals produced by radiation are particularly non-selective in the chemical structures which they attack. All we can say at the present time is that, while the initial interpretation of radiobiological data favoured the target theory and a direct action, the pendulum swung in recent years to the other extreme of indirect action, and a major role of active radicals. It is possible that now the pendulum is swinging back to a mid-position which suggests that even in the complicated systems of the intact cell, effects are produced by direct ionization of macromolecules, most certainly fortified or accentuated by the production of many active radicals from the water in the cell.

The Oxygen effect.

The radiosensitivity of cells as measured by a number of parameters is reduced by a factor of three if oxygen is absent from the environment during irradiation[10]. To be effective in restoring sensitivity oxygen has to be present during or immediately after the irradiation. Nitrogen at high pressure can compete with oxygen, and reduce sensitivity values to those of anoxia. It has now been established that, molecule for molecule, nitric oxide is as effective as oxygen in producing harmful effects[12].

Radiation and Carcinogenesis

One of the earliest observed biological effects of radiation was that of the production of cancer, yet today we do not know just how this conversion of a normal to a malignant cell is brought about by radiation. The somatic mutation theory is one of the attractive theories of the causation of cancer, and it is known that radiation produces mutations. In the production of leukemia in certain strains of mice by radiation it has been observed that the incidence of leukemia can be reduced by the injection of splenic cells, and practically prevented by the protection of 25% of the marrow by shielding. In some strains of mice it can be shown that the leukemia begins in the thymus. If the mice are irradiated, and subsequently the thymus removed and replaced by the thymus from a non-irradiated mouse, leukemia still appears[16]. The production of cancer by radiation seems to be a more

complex process than the mere hitting of chromosomes or certain loci in cells which subsequently become malignant.

The proponents of the virus theory of cancer have held that a cancer virus might exist in the body in a "pro-virus" form, which then might be unmasked by one of several mechanisms. It is known that certain viruses can reside in bacteria for many generations without the production of any observable effects, but by appropriate experimental conditions the virus can be activated and bring about the dissolution of the bacteria. One of the experimental factors which produces this effect is radiation, and there is a linear relation between radiation dose and lysogeny in bacteria, as there is a linear relation between dose and production of tumors in animals[30]. In view of the current interest in the role of virus in carcinogenesis, and the potency of agents such as those described by Stewart[27], the question of whether or not radiation may induce cancer by the unmasking of a virus is the subject of experiment in several laboratories.

Summary

We have considered some of the simple facts about ionizing radiation and cells, and how the two interact at the chromosome and macro-molecular level. We should view fundamental radiobiology as a fruitful source of experimental information about cells, as well as the basis for knowledge concerning protection against radiation.

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INFRAPULMONARY PLEURAL EFFUSION WITH PARTICULAR REFERENCE TO ITS OCCURRENCE IN NEPHROSIS*

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Ever since the classical articles of Damoiseau[4] and Ellis[5] in the middle and late 19th century respectively, the accepted concept of pleural effusion localization has been that the effusion first fills the costophrenic sinus laterally and posteriorly and then, as it increases in amount, gradually creeps up the thoracic wall, separating parietal from visceral pleura. The upper edge of this ascending fluid was said to be a percussable parabolic curve in the axilla, and came to be known as the Damoiseau-Ellis line. This curved line is still sometimes referred to, although subsequent investigations have shown that it is mythical. The concept of the typical pleural effusion accumulating as a meniscus with a concave upper surface surrounding the lung laterally and posteriorly has persisted in various degrees up to the present time. The cause of the peripheral distribution of the fluid and the exact shape of its upper edge were subject to experiment and debate from the time of the earliest use of the X-ray in diagnosis. An "atypical" collection of fluid was first described by Rigler[24] in 1931 in two cases, one of which was a child with nephrosis. In his cases the fluid overlaid the diaphragm, and had a convex upper surface, simulating elevation of the diaphragm. It could be demonstrated by placing the patient on his side in horizontal position, when it would move into the lateral pleural space and reveal itself in radiographs. Since then many reports of non-encapsulated pleural fluid collecting between the base of the lung and the diaphragm have been described, and have been called by several names including "reverse meniscus", "diaphragmatic effusion", and "infrapulmonary pleural effusion (I.P.P.E.)"[3,6,9,11,16,21,26,31,32,34]. In 1936 Rigler[25] published further observations on this phenomenon and included three cases of nephrosis, of which one had been recorded in his earlier reports. Since then in spite of considerable interest in I.P.P.E., we have been able to find in the available literature on this subject and on nephrosis, only five more cases of patients with nephrosis having demonstrable infrapulmonary effusion[1,6,9,32]. Our interest was aroused by what appeared to be a high incidence of I.P.P.E. in patients seen at the Montreal Children's Hospital in the active stages of the nephrotic syndrome.

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Methods and Materials

Of 75 patients who had been seen in this hospital since 1948 in the active stage of the nephrotic syndrome, 24 had had no chest X-rays made, and two more had had chest X-rays made when the nephrosis was not active.

The charts and chest X-rays of the remaining 49 patients were reviewed to determine whether there was any evidence on the films of I.P.P.E. 36 of these 49 cases (approximately 75%) were judged to show evidence of fluid between the base of the lung and the diaphragm on one or both sides, and 13 to show no such evidence. The 36 positive cases were then classified arbitrarily into slight, moderate and marked degrees of I.P.P.E. 12 cases showed slight changes, 18 moderate, and 6 cases showed a large collection of fluid. 9 effusions were unilateral and 27 bilateral (Table I). The positive cases were then surveyed with reference to characteristic features permitting the identification of I.P.P.E. The following signs were felt to be of importance in the identification of the fluid.

1. *"Reverse meniscus"*. This was present in all cases, and constitutes an essential part of the entity. It represents an elevation of the base of the lung in a relatively smooth curve with convexity upward, and therefore simulates in the upright position elevation of the diaphragm on one or both sides.

2. *Change in the contour of the lung base.* The convexity of the curve was consistently different from that seen in elevation of the diaphragm. The curve reached its maximum height at approximately the junction of its middle and lateral thirds rather than at its center, and the distal third tended to be more elevated than the medial third. This was found to be sufficiently characteristic in our material to constitute a reliable sign of I.P.P.E.

3. *Posterior fluid collection.* In the majority of cases careful inspection of the posterior costophrenic sinus in lateral or oblique projections showed a small amount of fluid ascending from the costophrenic sinus up the posterior chest wall, with the patient in upright position. This was absent only in cases where the amount of fluid was slight or minimal in degree. It therefore constituted a valuable sign of I.P.P.E.

4. *Separation of the stomach bubble from the left leaf of the diaphragm.* This was present in all cases where the effusion was present on the left side and where the stomach bubble could be identified. The normal stomach bubble however does not necessarily provide a reliable outline of the contour or height of the left leaf of the diaphragm. With this in mind, films of the chest were made before and after inflation of the stomach with gas in an essentially normal child (Fig. 1 A, B and C).

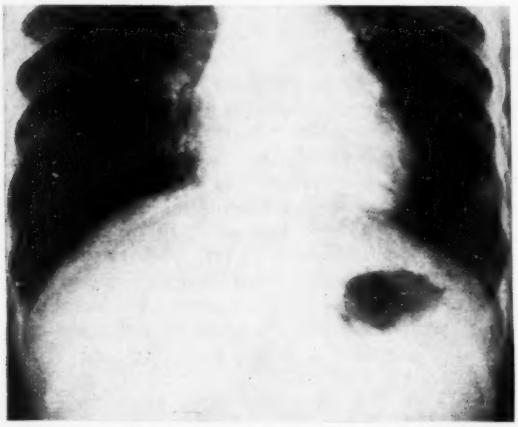


Figure 1 A. Normal chest film with separation of stomach bubble from diaphragm.

Figure 1 B. Lateral view showing that the apparent separation is caused by the projection of the high anterior portion of the diaphragm over the stomach.

5. *Shift of fluid with posture change.* This was investigated only in occasional cases for demonstration purposes, or when the diagnosis was in doubt. The left-side-down or right-side-down (so called lateral decubitus) position was found to be more reliable than the supine position. It was noteworthy that the shift in position of the fluid was not necessarily complete with change from erect to horizontal position. Depending on the size of the fluid collection, some separation of lung base from the diaphragm tended to persist in many cases, even with the patient horizontal.

Figure 1 C. After inflation of the stomach.

6. *Mediastinal effusion.* In some cases a characteristic sharply defined, thin mediastinal density was present in the left lower chest separating the lung from the mediastinum (Fig. 2). This represented fluid ascending along the mediastinal parietal pleura, and was always on the left side when present. It was seen in one of the 12 cases classified as slight, 6 of the 18 moderate cases, and in 1 of the 6 marked cases.

7. *Anterior costophrenic sinus.* It was noted that except in cases with large or massive effusions, or in cases where there was reason to suspect pleural adhesions, the anterior costophrenic sinus was clear, in contrast to the usual slight obliteration of the posterior sinus.

8. *Fluid in fissures.* A small amount of fluid was frequently seen in the lower end of one or both great fissures. No large interlobar effusion was seen.

Case Histories

The cases included in this review are all under the care of the Endocrinology Service of the Montreal Children's Hospital. The following case histories are representative.

Case 1. B.A. male, age 3½. This patient was admitted to The Montreal Children's Hospital in April 1953 with a history of swelling of the face and feet and fever of 101° for two days before admission. He had had repeated colds during the past year. The previous history was otherwise noncontributory. On examination, the patient was a pale edematous male child. There was edema of

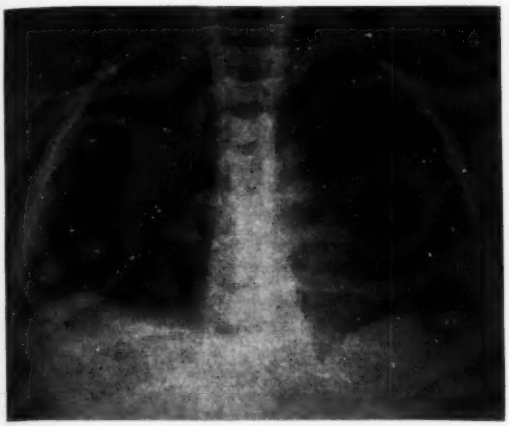


Figure 2. Case I. Classified as "moderate".
A. P.A. Typical "reverse meniscus" and lower left mediastinal fluid collection. The reproduction is over-exposed to make the left lower mediastinal triangular fluid collection more obvious.

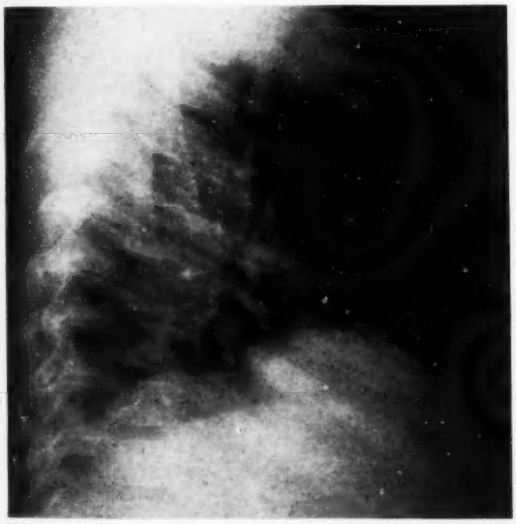


Figure 2 B. Lateral view showing a small fluid collection in the posterior sinus.

the face and pitting edema over the sacrum and lower extremities. There were signs of abdominal ascites. Hemoglobin was 11 grams, white blood count 6100, e.s.r. 26 m.m., urine albumin 1000 mgms., N.P.N. 48 m.g. per cent, serum proteins 4.7 grams percent (albumin 1.65, globulin 3.05). Chest radiograph on admission (Fig. 2) showed distension of the abdomen and I.P.P.E. with left-sided mediastinal pleural effusion. A diagnosis of acute nephrosis with upper respiratory infection was made. He was treated with antibiotics and dietary restrictions. Temporary improvement occurred but he was admitted on several occasions subsequently with recurrence of nephrosis, and finally died of peritonitis in August 1954.

Case 2. L.P. female, age 7. This child was apparently perfectly well until four to five weeks prior to admission when she developed fever. On one occasion the mother noticed blood in the urine. Two days before admission fatigue was noted and

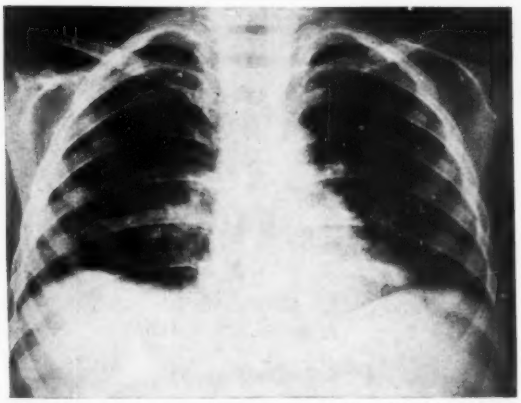


Figure 2 C. Normal exposure of PA film (A). The left lower mediastinal collection is recognizable, but not obvious.

concurrently swelling of the feet occurred. The family and past history were non-contributory. On physical examination on admission the patient was acutely ill with edema of the face, and legs up to the knees and over the sacrum. Temperature was 101° F., pulse 124. A grade 1 to 2 soft systolic murmur was heard over the left sternal border. Blood pressure was 140/115. Other physical findings were non-contributory. Hemoglobin was 8.5 grams, white blood count 6500, neutrophiles 4700, lymphocytes 1500. Urinalysis showed 15 to 20 red blood cells per high-power field and these became much more numerous sporadically on subsequent urinalyses. Urine albumin was approximately 500 to 800 mgms., and casts 2+. Serum total protein was 5.4 grams % (albumin 3.0, globulin 2.4), N.P.N. 40 mgm.%, serum sodium 124 m.Eq/L., potassium 3.9 m.Eq/L., chloride 120 m.Eq/L. Urine culture revealed no pathogens on admission, but later gram-positive cocci were grown. Chest radiograph (Fig. 3a) showed no pleural effusion on admission. Ten days later bilateral I.P.P.E. was present, more marked on the left. Films were done (Fig. 3b,3c,3d) in upright and left-side-down positions. A diagnosis of subacute nephritis with nephrotic component and hypertension was made. On discharge she was improved after treatment with steroids.

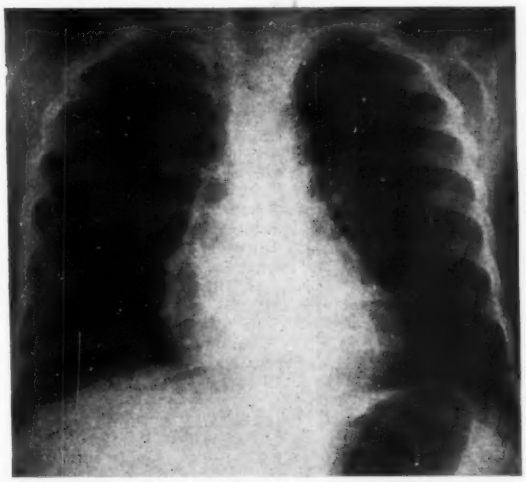
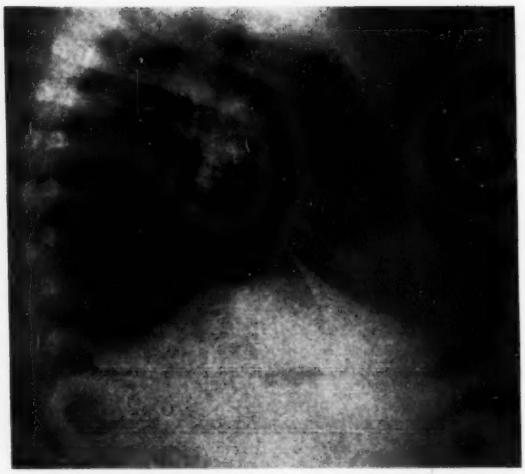


Figure 3. Case II. Classified as "moderate".
A. (P.A. chest film on admission). No effusion visible.



Figures 3 B. and C. (During the active stage). A small amount of fluid is visible in the left major fissure and bilateral I.P.P.E. A small but definite collection is visible in the posterior costophrenic sinus.

Case 3. J.M. male, age 8. This patient was well until two days before admission when he began to cough. On the day of admission he woke with a swollen face and puffy eyes. Swelling of the legs then appeared. He began to have crampy abdominal pain and then to vomit. Previous history was noncontributory except for a cold a few weeks previously, which had been treated with sulfonamide. On admission the physical examination showed generalized edema, normal temperature, pulse of 120, and no other significant findings. Urinalysis showed albumin 3500 mgm.%. Serum total protein was 4.6 grams %, (albumin 1.7, globulin 2.9), N.P.N. 54 m.g.%, cholesterol 499 mgm.%. Chest radiographs (Fig. 4) showed elevation of the base of each lung. due to I.P.P.E. This was confirmed by fluoroscopy by an A.P. film with the patient horizontal with left-side-down (left decubitus). The patient was treated with antibiotics and cortisone and on discharge was improved markedly.

Discussion

Following Rigler's report of the first recognized cases of I.P.P.E. in 1931, there have been numerous further case reports, noting its occurrence in tuberculosis, pneumonia, empyema, hemothorax, chylothorax, pleural lymphoma, metastatic carcinoma, and heart failure[10,12,21]. Since it can occur with a pleural transudate, exudate or hemorrhage, it appears clear that the infrapulmonary position of the fluid was not related to the actual physical properties of the fluid itself or even to the primary lesion responsible for it. Most authors have agreed that I.P.P.E. is much more common than generally realized, and that the more often one looks for it the more often it will be found. It is still not being found frequently in nephrosis. For example, Leuallen reviewed 436 cases with pleural effusion at the Mayo Clinic, and in analysing the causes, listed only 1 case of nephrosis[15].

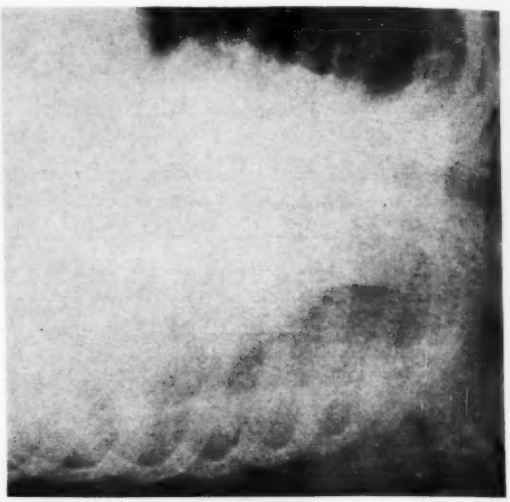


Figure 3 D. (P.A. view with left side down). The fluid has moved into the lateral pleural space.

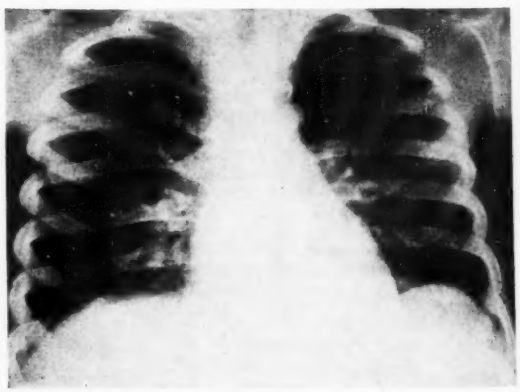


Figure 4. Case III. Classified as "moderate".
A. Frontal film. Bilateral I.P.P.E., more marked on the left.

Figure 4 B. Lateral. A posterior costophrenic sinus collection of fluid is visible.

Figure 4 C. P.A. film with the left side down. Fluid is visible in the pleural space on the dependent side.

Among the physical factors influencing the distribution of fluid in the pleural space the following have been cited:

1. Hydrostatic pressure of the fluid.
2. Retractility of the lungs.
3. Capillary action between fluid and pleural surfaces.
4. The physical properties of the fluid itself.
5. The physical properties of the pleural surfaces, and their alteration by adhesions or pleural thickening and rigidity.

Kaunitz[13] experimented with rabbits' lungs enclosed within a fluid-filled flask and a gas-filled flask in 1934. He showed that the contour of the upper border of the fluid between the gas-filled specimen and the inner surface of the jar was influenced by the degree of distension of the specimen (lung or balloon) and in particular its approximation to the inside of the flask. Paraf and Zivy[20] in 1939 injected up to 100 cc. of serum into the pleural space of a monkey. X-rays in upright position showed that this injected fluid collected between the base of the lung and the upper surface of the diaphragm as in I.P.P.E. When the animal was placed on its side the injected fluid spread along the thoracic wall. With the animal lying on the opposite side the fluid escaped from the infrapulmonary position to the mediastinal pleural space. They concluded as follows: providing the lung and pleura are healthy, pleural fluid will be localized between the diaphragm and the base of the lung. The fluid is capable initially only of lifting the lung, not separating it from the thoracic wall. Voluminous effusions are required to round the costophrenic sinus. At first the lower border of the lung is concave, then it tends to straighten out, and finally runs obliquely upward and outward. In inflammatory effusion such as tuberculous pleurisy, often the pleura is rigid and thick and basal adhesions may be present; the exudate therefore does not lift the lung, but rises around it.

In 1951 Hessen[9] published the results of a most careful and thorough investigation of the problem of the behaviour of pleural fluid as demonstrated by X-ray examination. He described cases of I.P.P.E. in patients with and without evidence of parenchymal changes in the lungs. Comparing these two groups of patients he established that loss of retractility of the lung is not responsible for the infrapulmonary situation of free pleural fluid. He performed a notable series of experiments with rabbits and human subjects and human corpses, again showing that loss of lung elasticity and contractility is not of major importance in the infrapulmonary localization of the pleural fluid. Since, as noted above, the character of the fluid itself can vary widely in different diseases where I.P.P.E. occurs, he concluded that localization of the fluid between the base of the lung and the diaphragm is the first and most normal event which occurs when fluid collects in the

pleural space for any reason, and that it assumes the more familiar "meniscus" or "mantle" appearance and ascends the thoracic wall only when it increases in quantity, or when pleural adhesions are already present, preventing the infrapulmonary localization. Hessen showed that the film made with "one-side-down" (lateral decubitus) is more efficient than the supine film in demonstrating small amounts of pleural fluid, and that the thickness of the layer of fluid demonstrated in this position is greater in expiration than in inspiration. He also showed that in a minority of normal individuals a small amount of physiologic pleural fluid is demonstrable, and is best shown with the patient in the left or right-side-down position, and with the head slightly lower than the feet. Hessen's work therefore amply confirmed the conclusions reached by Paraf and Zivy, and greatly enlarged our understanding of the dynamics of pleural effusion.

If, then, the I.P.P.E. is not at all "atypical" why is it not seen more frequently? Two reasons may be suggested. The first is that in many diseases where pleural fluid (whether pus, blood or transudate) is to be found, the pleura itself is abnormal and would tend to modify the distribution of the contained fluid because of the presence of adhesions, thickening, and rigidity. The second reason is that the increase in understanding of this phenomenon has not been paralleled by an increase in its appreciation in day-to-day clinical radiology. As long as I.P.P.E. is regarded as unusual or atypical, it will be recognized only rarely.

It has been stated[2,7,14,26] that routine X-ray examination of the chest will disclose pleural fluid only when it is present in amounts in excess of 250-400 cc. It should be recognized however that work in support of this concept has been done with the patient upright[13], and in fact generally with PA films only. It now becomes evident that the "masked" or hidden fluid is collected between the lung and the diaphragm. It will be revealed, even if present in very small amounts, if the patient is appropriately postured, and as Hessen has shown, particularly if the exposure is made during expiration.

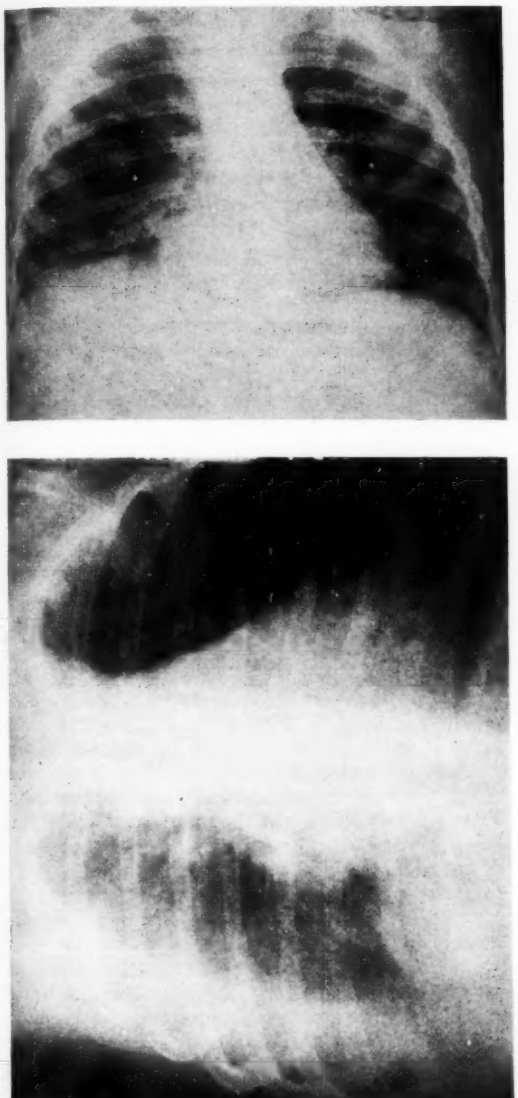
Our material would certainly appear to support the conclusions of Paraf and Zivy, and of Hessen. Out of a total of 49 children with the nephrotic syndrome x-rayed during the active stages of disease, approximately 75% showed signs of I.P.P.E. on review of the films. It seems quite likely that this figure is conservative, since in many of the cases the X-ray of the chest was done as a routine procedure and before our interest in the subject was aroused. Had each case been carefully examined for the presence of I.P.P.E., it appears almost certain that the percentage of positive cases would have been even higher. An example of this is seen in Fig. 6. The first examination of December 1957 showed an X-ray appearance which we now would regard as typical of moderate to marked bilateral I.P.P.E., with a small and typical left-sided mediastinal collection. This however was overlooked in our department. The child returned in September 1958 after our interest in this entity had been aroused. The films made at that time showed that although the changes typical of I.P.P.E. were in fact less obvious than originally, it was quite easily demonstrated by tipping the child to the right and taking an additional film (Fig. 6c).

Of the total of 36 positive cases, approximately 75% were bilateral, approximately 5% right-sided and 20% left-sided. This apparent preponderance of left-sided incidence is probably at least partially due to the greater ease of recognition of the left-sided effusion because of the separation of the stomach bubble from the base of the lung.

The characteristic change in the contour of the "false" diaphragmatic leaf, as seen by X-ray, to an asymmetric convexity with the apex displaced laterally has been reported by others[9]. As the basal effusion becomes larger, the curve tends to flatten laterally and finally the fluid rounds the lower lateral border of the lung and separates the lung from the lateral thoracic wall.

The high incidence of pleural effusion would seem from our experience to be the cause of apparent elevation of the diphragm in many cases of nephrosis. The ascites which characteristically accompanies the soft tissue edema of nephrosis does cause some displacement upward of the diaphragm but not nearly

Figure 6 A. Child age 3, in active nephrosis. P.A. chest film shows typical bilateral I.P.P.E., more marked on the left. Classified as "moderate".



Figures 6 B. and C. 2nd attack. Bilateral I.P.P.E., less obvious than in A, with a smaller collection on the left. This woould now have been classified as "slight". The right side down P.A. film shows fluid in the right pleural space.

to the degree which would be supposed from the false diphragmatic shadow. In the typical nephrotic patient the heart appears to be sunk low between the diphragmatic arches. It now seems evident that this is quite unlike what would be expected from bilateral diaphragmatic elevation, either because of paralysis or because of increased intra-abdominal contents. If the diaphragm were to ascend from either of these causes, the heart would be expected to assume a more transverse position, as it does in pregnancy or obesity. This "depressed" position of the heart in bilateral I.P.P.E. therefore is characteristic and should itself lead to recognition of the pleural fluid, as pointed out by Hessen[9].

Posterior costophrenic sinus blunting and small posterior chest wall effusion has been sufficiently frequent in this series to be of value in the identification of I.P.P.E. The very slight amount of posterior peripheral fluid shown on the oblique or lateral projection is quite consistent with Hessen's thesis that it represents a small proportion of the basal fluid collection escaping into the posterior peripheral pleural space. It is in striking contrast to the large amount beneath the lung. It is easy to miss, particularly because of the masking effect of the soft tissue edema (Fig. 2b). Occasionally it is large enough to be quite obvious (Fig. 4b).

We were interested to find that even in the lateral decubitus position enough of the fluid often remains between the lung and the diaphragm to simulate diaphragmatic elevation. In cases where the position of one leaf of the diaphragm is of critical importance in assessing the possibility of infra-diaphragmatic or supradiaphragmatic inflammatory disease, this becomes an important practical point. In a patient with fever and elevation of one leaf of the diaphragm, subphrenic inflammation may be suspected. An X-ray film made with the patient's affected side down may show that some of the apparent diaphragmatic elevation is due to pleural fluid, but some of the apparent elevation may persist. In such a case it is best to aspirate the fluid and then radiograph the chest again before assuming that any diaphragmatic elevation of significance is really present.

We did not attempt to make films in inspiration and expiration in our patients. Although Hessen demonstrated that small amounts of pleural fluid are better shown in expiration than in inspiration, this method does not lend itself well to use in a child with nephrosis. It is difficult to get good films in inspiration and expiration because of the child's poor condition and lassitude, and usually unnecessary, since the amount of fluid present is usually large enough to be readily demonstrated when once it has been suspected. Similarly, we did not use the technique suggested and demonstrated by Friedman, of inflating the stomach bubble to demonstrate the separation of the diphragm from the lung, though it may well be useful in the occasional difficult case. We were interested however, in the fact that although it is fairly widely recognized, none of the previous contributions in the literature contained a demonstration of the normal patient with apparent separation of the stomach from the lung and the

change in this appearance after inflation of the stomach. We have therefore included one such patient (Fig. 1) in this presentation.

The pleural effusion in nephrosis is probably not a major factor in discomfort or dyspnea in most cases. How much it really contributes to the patient's disability however, is unknown, since there has evidently been no previous appreciation of the high incidence of pleural effusion in this disease. It may be that further experience will provide more information about the desirability or otherwise of removal of the pleural fluid.

It is of considerable interest that there is almost no available information about the physical properties of normal or abnormal pleural fluid. It is known that the electrolytes in pleural fluid equilibrate very rapidly with those in the blood, but that equilibration between pleural fluid protein content and serum proteins is slow and incomplete. This has been shown to be due to absorption of fluid and molecules of low molecular weight across the pleural membrane directly into capillary blood. Absorption of the larger protein molecule is via the slower and more indirect route of pleural lymphatics[30]. One would expect then, that in a pleural transudate the viscosity, surface tension, and specific gravity of the fluid would be determined largely by its protein content. There is however, no reliable data on the physical characteristics of nephrotic pleural fluid. Since, as noted above, infrapulmonary fluid is seen in exudates and hemorrhage as well as transudates, one would not expect any considerable change in our present concept of I.P.P.E. to result from analysis of specimens for specific gravity, viscosity and surface tension, but until this is done in a considerable number of patients we must consider that the answer is not known. It is interesting that the only examination of the small amounts of pleural fluid which we now know to be demonstrable in some normal individuals[9] was done by Yamada[33], and even he obtained the fluid after exercising his subjects to the point of exhaustion; the fluid he obtained therefore may not have been normal in the strictest sense.

The triangular density in the left lower mediastinum which appeared in eight of our cases is quite characteristic of I.P.P.E., and appears to be reliable for its identification, though it has not been mentioned by previous authors. It simulates left lower lobe basilar segment collapse, but should not be difficult to distinguish from collapse or consolidation. It is thinner, better defined, and is continuous with the false "diaphragmatic" contour inferiorly and with the mediastinal border shadow superiorly, does not conform to the shape of any segmental collapse, and contains no "air bronchogram". If any confusion does occur, posturing the patient will show a characteristic change in the size and shape of the triangular mediastinal shadow. We were unable to explain the left-sided position of this mediastinal collection. In the upright position, we have never seen it on the right side. The amount of fluid present along the left lower mediastinum is always smaller than that which collects below the lung. The explanation for this is not entirely clear but may be simply that the lung is more readily displaced upward than it is laterally, due to its attachment at the hilus and the pulmonary ligament. Even with the patient postured with the affected side up, therefore, the amount of fluid collecting along the lower mediastinum is seldom large.

Review of our cases has not shown any relationship between the size or distribution of the infrapulmonary fluid and the prognosis of the nephrotic state. We have not analysed our cases statistically with respect to age distribution. Nephrosis occurs chiefly in early childhood, with a maximum incidence from age 2 to 5, and this was in a general way reflected in our series.

The X-ray appearance of the chest of a patient with nephrosis is quite characteristic. The combination of unilateral or bilateral I.P.P.E., with a normal sized heart which is depressed below the lung bases, and massive soft tissue edema, is readily recognized. In particular, it is the reverse in most respects from the appearance seen in patients with acute nephritis. In nephritis the heart is usually slightly enlarged, pleural effusion is very uncommon, and pulmonary edema, which is not seen in nephrosis (even in the presence of massive edema of all the soft tissues supplied by the systemic circulation) is very frequent in nephritis. We have therefore found it of interest to try to identify patients with the nephrotic syndrome from this characteristic X-ray appearance. Although interesting, the typical X-ray appearance cannot be regarded as valuable in the diagnosis of nephrosis, since the diagnosis is generally quite obvious from physical and laboratory examination.

The characteristic edema and pleural effusion and ascites seen in nephrosis are presumably closely related to the severe hypoproteinemia characteristic of the disease. With this in mind, we reviewed one case of congenital idiopathic hypoproteinemia. We were impressed by the marked similarity of the X-ray appearance in the two diseases.

Case 4. C.W. female, age 1½. This patient was admitted with a history of edema of the face and extremities with vomiting and diarrhea for 10 days. There was no fever, and no history of infection. There has been edema of the right arm since birth. Past history and family history were non-contributory. On physical examination the child showed normal development. The right upper extremity showed non-pitting edema. In addition there was generalized edema and abdominal distension. Pharyngitis was said to be present. Laboratory findings included hemoglobin 13 grams, white blood cells 11,000; urinalysis showed occasional casts, but no albumin. Serum protein was 4.3 mgm.%, (albumin 3.4, globulin 0.9) N.P.N. 19.6 mgm.%, serum cholesterol normal. Serum electrophoresis showed almost complete absence of gamma globulin, with marked reduction of beta-globulin and slight diminution of alpha I and II globulins. Serum albumin was within normal limits. The patient remained essentially unchanged except for a slight rise in the serum gamma globulin after treatment with gamma globulin, and intravenous fresh frozen plasma. She was discharged about one month after admission. The discharge diagnosis was idiopathic hypoproteinemia and congenital lymphedema of right upper extremity. Chest radiographs on three different occasions showed I.P.P.E., bilateral, indistinguishable from that seen in nephrosis (Fig. 5).

Summary

A review of 49 patients who had radiological examinations of the chest made during the active stage of the nephrotic syndrome has shown that approximately 75% of them had identifiable I.P.P.E. The previous literature contains case reports of 8 patients with nephrosis and I.P.P.E. Our material indicates that this association is the rule rather than the exception. The results of this review suggest that the incidence may in fact be higher than 75%, if I.P.P.E. is looked for in every case of active nephrosis.

TABLE I

Chest films made during active nephrosis

No evidence of pleural effusion	13	25%
Evidence of pleural effusion	36	75%
TOTAL	49	
Cases arbitrarily classified as slight	12	34%
moderate	18	50%
marked	6	16%
TOTAL	36	
Side involved was right	2	5%
left	7	20%
bilateral	27	75%
TOTAL	36	

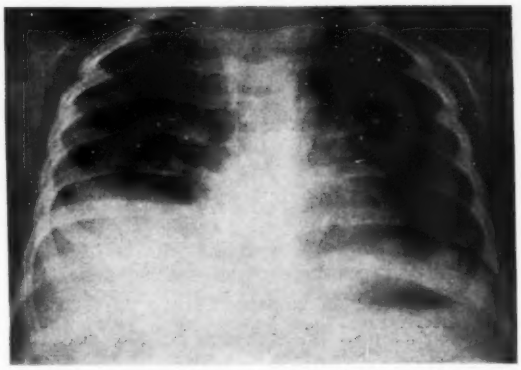


Figure 5. Case IV. Idiopathic Hypoproteinemia. Not included in Table I, but would be rated as "marked".
A. Upright.

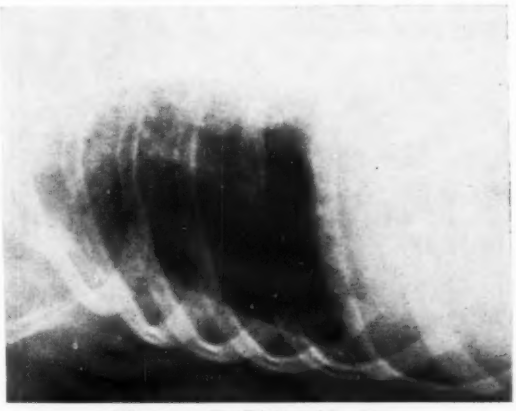


Figure 5 B. Right side down.

In nephrosis the I.P.P.E. is bilateral in approximately 75% of cases when it is present, and although perhaps more common on the left side than on the right, it is harder to identify on the right, particularly when unsuspected.

Our conclusions are in entire agreement with those of Hessen and others who have found on both clinical and experimental grounds that the infrapulmonary position of pleural fluid is the normal one, and that the more easily recognized "meniscus" appearance only occurs when the fluid collection is massive enough to progress from its infrapulmonary position up the lateral chest wall, or when pleural adhesions are present to limit the available space between the base of the lung and the diaphragm.

We have not found any relation between the size of the effusion and the ultimate prognosis of patients with nephrosis.

Chest films of patients with nephrosis have a rather typical and recognizable appearance including soft tissue edema, unilateral

or bilateral I.P.P.E., and a low position of the heart relative to the bases of the lungs. This same appearance may be expected in severe hypoproteinemia from other causes, as shown by a single case of congenital hypoproteinemia.

I.P.P.E. can be recognized by any of the following changes;

Reverse meniscus.

Change in contour of the lung base.

Fluid in the costophrenic sinus posteriorly.

Separation of the stomach bubble from the left leaf of the diaphragm.

Displacement of fluid with posture change, including displacement into the dependent pleural space laterally in the "lateral decubitus" position.

A characteristic left lower triangular mediastinal fluid collection, which was found in 8 of our cases, and has not been previously described.

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THE DOBBIE VERTICAL PLANE FINDER

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Ontario Cancer Foundation
Kingston, Ontario

THE DEVICE, to be described below, is of considerable value in teaching the steps in setting up a treatment field. It is also of practical value in enabling an unusually directed field to be set up with least difficulty.

The Dobbie Vertical Plane Finder consists essentially of an enclosed hemisphere inside which a small spherical ball is free to roll. The motion of the ball is damped by filling the hemisphere with mineral oil before sealing. The hemisphere is contained in a rectangular plastic container, so that the plane face of the hemisphere is parallel to the bottom of the container. The corners at the bottom have been rounded off to facilitate the placing of the device on more difficult sites. The device is illustrated in Figure 1. A meridian is engraved on the hemisphere and degrees of tilt marked off from 0° to 90°, 0° being at the bottom of the hemisphere and 90° at the edge.

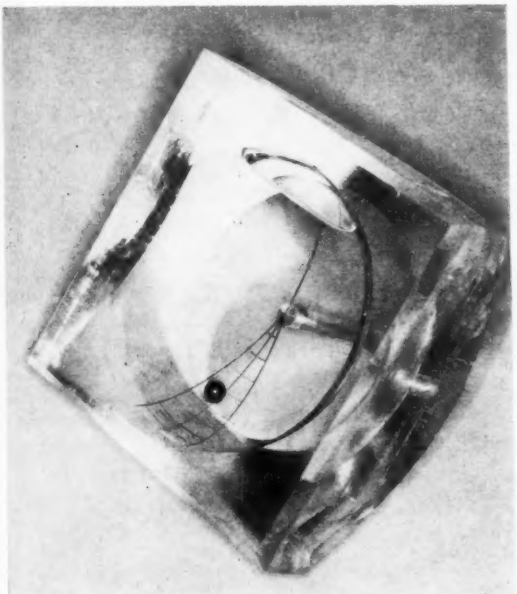

Figure 1. The Dobbie Vertical Plane Finder inclined at an angle of 45°.

Many tube-heads are provided with two axes of rotation to enable the treatment cone to be applied in various directions. However, when setting up a treatment field the adjustment of one angle of rotation usually requires correction of the other angle also and this can only be done by a procedure of trial and error. Such is difficult to reproduce accurately in repeated treatments. It is our preference to use only the main axis of rotation, as any area can be treated without the other movement as described below.

As the tube-head swings through its main axis the central ray describes a line on the floor as illustrated in Figure 2. If the Vertical Plane Finder is placed on the treatment area

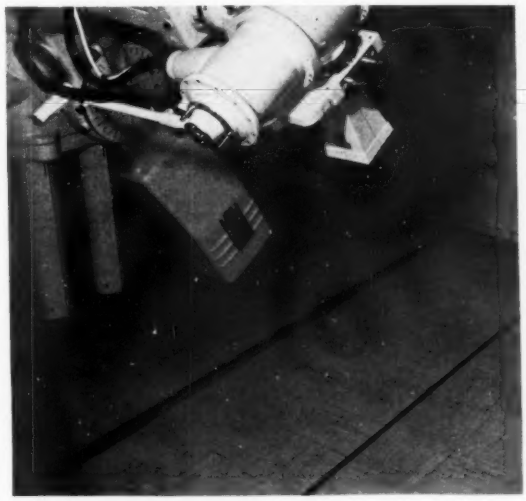

Figure 2. Shows the tube head tilted at an angle of 30° about its main axis. The black line on the floor is that described by the central ray on rotation.

Figure 3. The ball is lying on the meridian at the third division indicating that the tube head must be angled 30° from the vertical. The patient must be rotated until this meridian lies over the line on the floor.

and rotated until the ball rests on the meridian, then this meridian describes a vertical plane of the treatment area. Move the treatment table until the meridian lies over the line on the floor. The tube-head must now be rotated until the angle of the cone from the vertical is the same as the angle that the ball indicates on the meridian. By a horizontal movement of the table and a lowering of the tube-head, the cone can now be placed easily in the correct position. The Vertical Plane Finder is seen in operation in Figure 3.

It can be noted that the elimination of one axis of rotation of the tube-head greatly reduces the protection requirements of the room.

ACKNOWLEDGMENTS: This is a modification of an apparatus using a plumbline and protractor designed by Dr. J. L. Dobbie of the Christie Hospital, Manchester, England. This modification grew out of a suggestion by Dr. Wayne Whitcomb, St. Raphael's Hospital, New Haven, Conn.

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